(c) at least one transcription enhancer;

B4 Cont (d) a negative regulatory element;

(e) at least one hormone responsive element;

(f) at least one avian CR1 repeat element; and

(g) a proximal lysozyme promoter and signal peptide-encoding region.

B5 29. (Amended) The expression vector of Claim 22, wherein the nucleic acid insert has one or more codons optimized for protein expression in an avian.

B6 58. (Amended) The recombinant DNA molecule of Claim 8, wherein the nucleic acid insert has one or more codons optimized for protein expression in an avian.

REMARKS

Claims 1-7 have been canceled without prejudice and Applicant reserves the right to prosecute the canceled subject matter in a related application. After entry of this amendment, Claims 8-61 will be pending. Claims 1-57 were subject to a restriction and/or election requirement. Claims 58-61 were not considered by the Examiner because, according to the Examiner, Claims 58-61 are unclear. Claims 8, 17, 22, 29 and 58 have been amended to more particularly point out and distinctly claim that which Applicant regards as the invention. In particular, Claims 8 and 22 have been amended to make clear that the nucleic acid insert encodes a heterologous (*i.e.*, a non-lysozyme) polypeptide. Support for this amendment can be found in the specification, at page 47, lines 3-5. Claim 17 has been amended to correct a grammatical error. Claims 27 and 58 have been amended to make clear that the nucleic acid insert has codons optimized for protein expression in an avian and Claim 58 has also been amended to make it dependent on Claim 8. Support for these amendments can be found in the specification, at page 44, line 7 to page 45, line 20. No new matter has been added by these amendments. A marked-up version of the amended claims to show changes made by the current amendment is attached hereto as Exhibit B. The Abstract was also amended in response to the Examiner's objection that the Abstract is greater than 250 words. In response, Applicant has amended the Abstract to be in compliance with the 150 word limit of 37 C.F.R. 1.72. No new matter has been added by these amendments.

I. CLAIMS 58-61

Applicant respectfully requests that the Examiner consider Claims 58-61. The Examiner asserted that Claims 58-61 are unclear. In response, Applicant has amended Claim 58 to depend upon Claim 8 and make clear that a nucleic acid insert, to which an avian lysozyme gene expression control region is operably linked, has one or more codons optimized for protein expression in an avian. Optimization of codons for protein expression is taught in the specification in the section entitled "Codon-optimized proteins" (see page 43, line 1 *et seq.*). Generally, each species may preferentially utilize certain codons in their protein sequences and their cellular components, e.g., percentages of each tRNA, may reflect this preference. To efficiently express a non-avian protein in an avian cell, it may be desirable to optimize the nucleic acid insert sequence such that its codons correspond to those preferentially utilized in avian cells.

Applicant submits that Claim 58, as amended, is clear and that, therefore, dependent Claims 59-61 are also clear. Applicant respectfully requests that the Examiner consider Claims 58-61. As these claims are dependent upon Claim 8, Applicant submits that Claims 58-61 belong in Group I, described below, and respectfully requests that the Examiner consider Claims 58-61 as part of Group I.

II. RESTRICTION REQUIREMENT

The Examiner has required a restriction under 35 U.S.C. § 121 to one of the following inventions:

Group I	Claims 1-33, drawn to an isolated nucleic acid sequence comprising an avian lysozyme gene expression control region;
Group II	Claims 34-36, drawn to a method of expressing a heterologous polypeptide in a host cell *in vitro;*
Group III	Claims 34-36, drawn to a method of expressing a heterologous polypeptide in a host cell *in vivo*;
Group IV	Claims 37-39 and 41-44, drawn to a eukaryotic cell transformed *in vivo* with an expression vector;
Group V	Claims 37-40 and 42-44, drawn to a eukaryotic cell transformed *in vitro* with an expression vector;
Group VI	Claims 45-57, drawn to a transgenic avian.

The Examiner has further required an election of one of the following nucleic acid sequences:

A) SEQ ID NO: 67;

B) SEQ ID NO: 68;

C) SEQ ID NO: 66; or

D) SEQ ID NO: 65.

In order to be fully responsive, Applicant hereby provisionally elects the invention of Group I, claims 1-33, drawn to an isolated nucleic acid sequence comprising an avian lysozyme gene expression control region, classified in class 536, subclass 24.1, and further provisionally elects the nucleic acid sequence of SEQ ID NO: 67, with traversal. Applicant respectfully requests that the Examiner include Claims 58-61 in group I for the reasons set forth above.

With respect to the Examiner's division of the invention into six groups and the reasons stated therefor, Applicant respectfully traverses.

Even assuming arguendo that Groups I-VI represented distinct or independent inventions, Applicant submits that to search the subject matter of all the Groups together would not be a serious burden on the Examiner.

The M.P.E.P. § 803 (Eighth Edition, August 2001) states:

> If the search and examination of an entire application can be made without serious burden, the examiner must examine it on the merits, even though it includes claims to distinct or independent inventions.

Thus, in view of M.P.E.P. §803, all of Claims 1-61 should be searched and examined in the subject application.

Accordingly, Applicant respectfully requests that the Restriction Requirement under 35 U.S.C. §121 be withdrawn and the instant claims be examined in one application.

Applicant fully reserves all right to prosecute the subject matter of any non-elected claims in one or more subsequent related applications. Applicant also retains the right to petition from the restriction requirement under 37 C.F.R. § 1.144.

CONCLUSION

Applicant respectfully requests that the foregoing amendments and remarks be entered and made of record in the file history of the application.

Respectfully submitted,

Date February 11, 2003

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EXHIBIT A

Application No. 09/922,549 filed August 3, 2001

MARKED-UP VERSION TO SHOW CHANGES MADE IN SPECIFICATION

February 11, 2003

The abstract has been amended as follows:

The present invention provides [novel] isolated nucleic acids comprising an avian [nucleic acid sequence encoding a] lysozyme gene expression control region operably linked with a nucleic acid sequence encoding a heterologous polypeptide. The [isolated nucleic acid of the] present invention is useful for reducing the chromosomal positional effect [of a transgene operably linked to the lysozyme gene expression control region and] when such a nucleic acid is expressed [transfected into a recipient cell and allows expression of an operably linked heterologous nucleic acid insert] in a transfected avian cell[such as, for example, an oviduct cell]. [The isolated avian lysozyme of the present invention may be operably linked with a selected nucleic acid insert, wherein the nucleic acid insert encodes a polypeptide desired to be expressed in a transfected cell.] The nucleic acids [acid insert] may additionally comprise [be placed in frame with] a signal peptide sequence [, whereby translation initiation may start with the signal peptide and continue through the nucleic acid insert, thereby producing an expressed polypeptide having the desired amino acid sequence. The recombinant DNA of the present invention may further comprise] or a polyadenylation signal sequence. The sequence of the expressed nucleic acid insert is optimized for chicken codon usage. [This may be determined from the codon usage of at least one, and preferably more than one, protein expressed in a chicken cell.] The present invention further includes expression vectors comprising an isolated avian lysozyme gene expression control region of the present invention, and transfected cells and transgenic avians comprising the expression vectors.

EXHIBIT B

Application No. 09/922,549 filed August 3, 2001

MARKED-UP VERSION TO SHOW CHANGES MADE IN CLAIMS

February 11, 2003

8. (Amended) A recombinant DNA molecule comprising an isolated avian lysozyme gene expression control region operably linked to a nucleic acid insert encoding a heterologous polypeptide, wherein the lysozyme gene expression control region comprises:

(a) at least one 5' matrix attachment region;

(b) an intrinsically curved DNA region;

(c) at least one transcription enhancer;

(d) a negative regulatory element;

(e) at least one hormone responsive element;

(f) at least one avian CR1 repeat element; and

(g) a proximal lysozyme promoter and signal peptide-encoding region.

17. (Amended) The recombinant DNA molecule of Claim 16, wherein the nucleic acid insert encoding [the] an interferon α2b polypeptide comprises the sequence in SEQ ID NO: 66, or a degenerate variant thereof.

22. (Amended) An expression vector that integrates into a host cell and comprising an isolated avian lysozyme gene expression control region operably linked to a nucleic acid insert encoding a heterologous polypeptide, wherein the expression control region directs production of a transcript, wherein the lysozyme gene expression control region comprises:

(a) at least one 5' matrix attachment region;

(b) an intrinsically curved DNA region;

(c) at least one transcription enhancer;

(d) a negative regulatory element;

(e) at least one hormone responsive element;

(f) at least one avian CR1 repeat element; and

(g) a proximal lysozyme promoter and signal peptide-encoding region.

29. (Amended) The expression vector of Claim 22, wherein the nucleic acid insert has one or more codons [encoding a polypeptide has a codon complement] optimized for protein expression in an avian.

58. (Amended) The recombinant DNA molecule of Claim 8, wherein the nucleic acid insert has one or more codons [An isolated nucleic acid having a codon complement] optimized for protein expression in an avian.